REMARKS

Status of Application

Claims 1-7 were pending and claims 3-7 were withdrawn from consideration.

By this amendment, claims 1-2 are cancelled and new claims 8-19 are submitted. No new matter is introduced by these amendments.

Applicant requests reconsideration and allowance of claims 8-19, and rejoinder of appropriate method claims.

Applicant reserves the right to prosecute any withdrawn, canceled, or non-elected claims and/or subject matter in separate applications.

35 U.S.C. § 103 Rejections

Preliminarily, new claims 8-19 do not contain a limitation as to the oxygen content of a calcitonin salmon nasal spray as did cancelled claims 1-2. Thus, this issue has been mooted.

Examiner rejected claims 1-2 as obvious over APC (EP 0 115 627) (hereinafter, "EP '627") in combination with Azria et al. (U.S. Patent No. 5,759,565, issued 1968) (hereinafter, "the '565 patent"). Examiner stated in the Office Action mailed May 30, 2007 that Azria teaches that chlorobutanol at 0.6% "has a deleterious effect but is silent at lower concentrations." Examiner further stated that "Azria makes a case for a single point (concentration)." Examiner also stated that "EP '627 teaches these lower concentrations."

Applicant respectfully responds that Examiner has not supplied a *prima facie* case for obviousness because Azria et al. teach away from use of chlorobutanol in a calcitonin solution. Applicant respectfully submits that Examiner ignores the factual teaching of Azria et al., as discussed in previous papers, that chlorobutanol showed insufficient activity against a test fungus. The single point concentration recited in the '565 patent of Azria et al. was a sufficient basis to Azria et al. *themselves* as being a reason not to select chlorobutanol.

In view of the fact, as stated in Azria et al., that many possible preservatives could have been selected for testing in a calcitonin solution, yet only chlorobutanol was shown to be questionable, a person of ordinary skill in the art would not have been motivated to select and test chlorobutanol for use as a preservative in a calcitonin solution, regardless of other factors. The reference EP '627 is not pertinent to this issue since it provided no specific factual evidence on which a person of ordinary skill in the art could have relied in 1998 when the unsuitability of

chlorobutanol was factually shown by Azria et al. Thus, Applicant respectfully submits that a person of ordinary skill in the art in 1998 would not have been motivated to select and test chlorobutanol as a preservative in a calcitonin solution in view of Azria et al. In sum, the specific factual teaching of Azria et al. is that chlorobutanol is doubtful as a preservative, but benzalkoniumn chloride works well. This teaches away from selecting chlorobutanol for testing as a preservative in a calcitonin solution.

The above questions having been answered, Applicant respectfully submits that Applicant's discovery that chlorobutanol is suitable as a preservative in a calcitonin solution is an unexpectedly advantageous result. In support, Applicant submits the Declaration of Henry R. Costantino Under 37 C.F.R. § 1.132 herewith.

In his Declaration, Dr. Costantino shows representative data from a study of antimicrobial effectiveness testing of calcitonin salmon nasal spray samples of Applicant's invention for which the chlorobutanol content ranged from 0.125% to 0.5%. In sum, the results showed that chlorobutanol at a concentration of 0.25% in a calcitonin solution was acceptable to submit for passing USP criteria for antimicrobial effectiveness testing.

Dr. Costantino further declares that a person of ordinary skill in the art in 1998 would have known in general that a preservative is less effective against microbes when used at a lower concentration. It would therefore have been doubted by a person of ordinary skill in the art in 1998 based on the teachings of Azria et al. that chlorobutanol at any concentration less than 0.6% would have been useful as a preservative in a calcitonin nasal pharmaceutical composition. In other words, the alleged silence of Azria et al. regarding lower concentrations is moot in view of the teaching Azria et al. supplied to a person of ordinary skill in the art. Applicant respectfully requests that Examiner consider that it is the reasonable expectation of success of a person of ordinary skill in the art in 1998 that is at issue. That expectation did not exist in 1998 for chlorobutanol because of the factual teaching Azria et al.

Lastly, Dr. Costantino states that the results of antimicrobial effectiveness testing of calcitonin salmon nasal spray samples of Applicant's invention showed that chlorobutanol at a concentration of 0.25% was unexpectedly advantageous as a preservative in view of the teachings of Azria et al.

In view of the unexpectedly advantageous properties of Applicant's calcitonin salmon nasal spray, Applicant respectfully requests reconsideration and allowance of claims 8-19, and allowance and rejoinder of appropriate method claims.

Should there remain any unresolved issue that would require an adverse action, it is respectfully requested that Examiner telephone Applicant's attorney so that such issue may be resolved as expeditiously as possible.

Should the U.S. Patent and Trademark Office determine that any additional fee is due, or that a refund is owed for this application, the Commissioner is hereby authorized and requested to charge the required fee and/or credit the refund owed to Deposit Account No. 502769.

Respectfully submitted,

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